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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/739,089	12/15/2000	Constantinos Balas	FRN-002	3243

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EXAMINER
NERBUN, PETER P

ART UNIT	PAPER NUMBER
3765	

DATE MAILED: 02/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

N.K.

Office Action Summary	Application No.	Applicant(s)	
	09/739,089	BALAS, CONSTANTINOS	
	Examiner	Art Unit	
	Peter P Nerbun	3765	

-- The MAILING DATE of this communication app ars on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

On page 15, line 11 of the specification, an inadvertent syntax error should be corrected (the adjective "remitted" must modify a noun). Presently, there is no noun immediately following "remitted".

Applicant requests that the examiner indicate that the pending claims as allowable and declare an interference. Applicant further states that claims 18-34 of the U.S. patent application corresponding to U.S. Application Publication Number 20020007122 A1 have been found allowable by the examiner of the patent application corresponding to that publication number and that a Notice of Allowance was mailed in connection with this application. Applicant provides an Appendix B to paper no. 12 which applicant states is a copy of the first Office action in SN 09/738,147 (corresponding to U.S. Publication Number US 20020007122 A1).

In accordance with MPEP 2305.04, the examiner may suggest one or more claims for the purpose of interference with an application in issue to an applicant whose application is pending before him or her. MPEP 2305.04 further states that the examiner may write a letter suggesting claims to an applicant whose application is in issue when an application pending before the examiner contains one or more claims defining an invention to which claims may be presented in that application in issue. Such letters must be submitted to the TC Director for approval. The examiner will discuss these issues with his supervisor at the earliest possible time subsequent to the mailing of the instant Office action. Claim 18 of U.S. Application Publication Number 20020007122 A1 recites a method of diagnosing disease in a patient, the method including the step of dispensing a chemical agent on a tissue and providing an

automated triggering signal to initiate a measurement period relative to said dispensing step and measuring a temporal evolution of an optical signal observed from said tissue during said measurement period. The examiner has determined that the instant application has sufficient disclosure to support this claim. In particular, note page 13, lines 34-38, page 14, lines 1-6, and page 17, lines 29-37 of applicant's specification. Further, in the instant application, the examiner notes that U.S. Application Publication Number 20020007122 A1 has disclosure to support the copying of claim 1 of the instant application. This disclosure is contained on page 6, paragraph [0072] and page 11, paragraph [0114] of U.S. Application Publication Number 20020007122 A1. Should the discussion between the examiner and his supervisor lead to the suggestion of a claim by the examiner for the purpose initiating an interference this will not stay the period for response to any outstanding Office action.

On page 19, last paragraph of paper no. 12, applicant disagrees with the examiner's characterization of claim 1 of U.S. Publication Number US 2002/0127735 A1 as being different from Applicants claim 1. Claim 1 of U.S. Publication Number US 2002/0127735 A1 recites "dispensing a plurality of chemical agents on a tissue, wherein the chemical agents interact to alter an optical signal produced by the tissue" whereas applicant's claim 1 recites "applying a pathology differentiating agent on a tissue sample, wherein said pathology differentiating agent chemically interacts with said tissue sample and alters its optical characteristics". The examiner remains unconvinced that the case law cited regarding use of the indefinite article "a" or "an" has any pertinence with regard to claim 1 of the instant application. However, this point is

deemed moot because the examiner has located disclosure within applicant's specification to support a claim directed to "dispensing a plurality of chemical agents on a tissue, wherein the chemical agents interact to alter an optical signal produced by the tissue". In particular, on page 7, lines 4-7 of applicant's specification, applicant discloses a method including "contacting a tissue in a subject with a pathology differentiating agent, e.g. an acetic acid solution **or a combination of solutions selected from a plurality of acidic an basic solutions**,..." (emphasis added). Further on page 7, lines 17-20, applicant's specification discloses that a combination of agents may interact with pathologic tissue areas characterized by an altered biochemical composition. Thus while applicant does have disclosure to support the copying of claim 1 of U.S. Publication Number US 2002/0127735 A1, there is no indication on the record that claim 1 of U.S. Publication Number US 2002/0127735 A1 is allowable. To the contrary, applicant provides an Appendix B to paper no. 12 which applicant states is a copy of the first Office action in SN 09/738,147 (corresponding to U.S. Publication Number US 2002/0127735 A1). In that copy which applicant provides, claim 1 is seen to have been rejected over prior art. The copy that applicant provides indicates that only claims 18-34 have been allowed over the prior art of record. Therefore claim 1 could not serve as a count of any potential interference proceeding. Note MPEP 2301.01, paragraph "C" which states that "Before a claim (unless it is a patented claim) is considered as the basis for the count of an interference, the claim should be allowable and in good form.".

With regard to the examiner's evaluation of the Declaration under 37 CFR 1.131 (see paper no. 11), applicant states that the Journal of Photochemistry and Photobiology article submitted by applicant as evidence to establish prior invention does describe the step of monitoring the rate of change of light reflection from a tissue sample over time, thereby monitoring the effects of a pathology differentiating agent on the tissue sample. In this regard applicant should note that 37 CFR 1.131(b) requires that original exhibits of drawings or records, or photocopies thereof, accompany and form part of the affidavit or declaration or their absence satisfactorily explained. In Ex parte Donovan, 1890 C.D. 109, 52 O.G. 309 (Comm'r Pat. 1890) the court stated. If the applicant made sketches he should so state, and produce and describe them; if the sketches were made and lost, and their contents remembered, they should be reproduced and furnished in place of the originals. The same course should be pursued if the disclosure was by means of models. If neither sketches nor models are relied upon, but it is claimed that verbal disclosures, sufficiently clear to indicate definite conception of the invention, were made the witness should state as nearly as possible the language used in imparting knowledge of the invention to others. The affidavit or declaration and exhibits must clearly explain which facts or data applicant is relying on to show completion of his or her invention prior to the particular date. Vague and general statements in broad terms about what the exhibits describe along with a general assertion that the exhibits describe a reduction to practice "amounts essentially to mere pleading, unsupported by proof or a showing of facts" and, thus, does not satisfy the requirements of 37 CFR 1.131(b). In re Borkowski, 505 F.2d 713, 184 USPQ 29 (CCPA

1974). Applicant must give a clear explanation of the exhibits pointing out exactly what facts are established and relied on by applicant. 505 F.2d at 718-19, 184 USPQ at 33. See also In re Harry, 333 F.2d 920, 142 USPQ 164 (CCPA 1964). (Affidavit "asserts that facts exist but does not tell what they are or when they occurred."). In applicant's Declaration under 37 CFR 1.131 applicant has not presented any original exhibits of drawings or records, or photocopies thereof. Accordingly, the Declaration under 37 CFR 1.131 is incomplete and therefore inadequate to establish possession of the claimed invention. See MPEP 715.05. To support applicant's assertion that the Journal of Photochemistry and Photobiology article does describe the step of monitoring the rate of change of light reflection from a tissue sample over time, thereby monitoring the effects of a pathology differentiating agent on the tissue sample, applicant states that the article teaches that '"[i]n order to improve the sensitivity and specificity of clinical diagnosis we have quantitatively assessed, in vivo, the acetic acid-induced *temporal* and spatial alterations in the light scattering properties of abnormal epithelium by means of a specially developed imaging system" (Emphasis added; See page 154, right column, lines 8-12)'. Applicant notes that the term "temporal" is well known to mean 'of or relating to the sequence of time'. In response to this argument the examiner notes that the step of monitoring the **rate of change** of light reflection from a tissue sample over time, thereby monitoring the effects of a pathology differentiating agent on the tissue sample, is not disclosed by mere reference to a temporal assessment of acetic acid-induced alterations in light scattering properties of a tissue sample (emphasis added). The rate of change of light reflection from a tissue sample over time is the

change of light reflection intensity with respect to time over time. In terms of the differential calculus this rate of change is functionally defined as the first derivative of the magnitude of light reflection with respect to time (dR/dT) where "R" is the intensity of light reflection and "T" is time. Thus the step of monitoring the rate of change of light reflection from a tissue sample over time involves monitoring the first derivative of light reflection intensity over time. The step of making a temporal quantitative assessment of acetic acid-induced alterations in light scattering properties of a tissue sample involves the quantitative determination of the magnitude of the alterations, not the rate of change of such alterations. The same comment applies to applicant's reference to pages 155, 156, and 157 of the Journal of Photochemistry and Photobiology article.

With regard to the examiner's evaluation of the Declaration under 37 CFR 1.132 (see paper no. 11), applicant states that the Declaration under 37 CFR 1.132 does not only offer opinion testimony on the ultimate legal conclusion at issue. Rather, applicant states, the declaration offers statements of fact describing the contribution of each of the authors to the publication in the Journal of Photochemistry and Photobiology (e.g. that George C. Themelis was a graduate student in Dr. Balas' lab who performed technical aspects described in the publication under Dr. Balas' direction and supervision). The fact that Mr. Themelis was a graduate student in Dr. Balas' lab who performed technical aspects described in the publication under Dr. Balas' direction and supervision does not in itself establish facts leading to the conclusion that Mr. Themelis did not perform acts independent of Dr. Balas, such acts being related to making a determination of whether Mr. Themelis is a co-inventor. In the course of directing and

supervising Mr. Themelis, for example, did Dr. Balas personally direct and observe every action of Mr. Themelis? Applicant's Declaration under 37 CFR 1.132 does not provide facts necessary to answer this question. The same comments apply to the other co-authors of the publication.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaufman et al (U.S. Patent Application Publication No. US 2002/0127735 A1), taken as applied in the previous Office action. The patent application publication to Kaufman et al discloses a method for monitoring the effects of a pathology differentiating agent on a tissue sample, comprising: applying a pathology differentiating agent (see page 1, lines 3-6 of paragraph [0006]), wherein said pathology differentiating agent chemically interacts with said tissue sample and alters its optical characteristics; and monitoring the rate of change of light reflection from said tissue sample over time (see page 6, paragraph [0072] and page 11, paragraph [0114]), thereby monitoring the effects of a pathology agent on a tissue sample.

Claims 6, 7, 9-13 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Richards-Kortum et al, taken as applied in the previous Office action

(paper no. 11). The patent to Richards-Kortum discloses a method for the *in vivo* diagnosis of a tissue abnormality in a subject comprising contacting a tissue in a subject with a pathology differentiating agent (see col. 2, lines 44-46), wherein said pathology differentiating agent chemically interacts with said tissue sample and alters its optical characteristics (see col. 2, lines 47-48), exposing said tissue in said subject to optical radiation (see col. 1, lines 47-48), and monitoring the intensity of light emitted from said tissue over time by imaging the cells at a near real-time rate of image capture (note col. 1, lines 60-62 and col. 4, lines 52-63 which state that imaging can be used to obtain **near real-time** reflected light **images** of human epithelial tissue *in vivo* and that imaging of cells may be done **after** the application of acetic acid to the diagnostic tissue sample -- emphasis added). Further note col. 4, lines 45-48 which state that Richards-Kortum presents **images** as they appear at the time of acquisition without any post-processing and that these images are representative of what would be possible for clinical applications requiring **near video rate imaging** (emphasis added)). One having ordinary skill in the art would recognize that "near video rate imaging" constitutes image capture at a rate of multiple images per second. These multiple images acquired over time are displayed on a computer monitor (see col. 1, lines 47-54) which permit the clinician to monitor the intensity of light emitted from the tissue over time as recited by applicant in claim 6, line 6.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Richards-Kortum et al in view of Zavislan, newly cited. To utilize polarized optical radiation in the method of Richards-Kortum as suggested by Zavislan (at col. 2, lines 18-20) would have been obvious since Zavislan states this technique results in a reduction in the amount of surface reflection.

Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richards-Kortum et al. The particular type of tissue to which the tissue may be exposed (ear, esophagus, etc.) could have been selected in an obvious manner since Richards-Kortum et al state that their method applies to multiple tissue types and should be useful for improving contrast in a variety of organ sites (see col. 4, lines 36-41).

Applicant's arguments filed January 30, 2003 have been fully considered. On page 14, last paragraph of paper no. 12, applicant states that Richards-Kortum et al does not teach or suggest monitoring the intensity of light emitted from the tissue over time. The examiner disagrees. As previously noted, col. 1, lines 60-62 and col. 4, lines 52-63 of the disclosure of Richards-Kortum et al state that imaging can be used to obtain **near real-time** reflected light **images** of human epithelial tissue *in vivo* and that imaging of cells may be done **after** the application of acetic acid to the diagnostic tissue sample (emphasis added). Further col. 4, lines 45-48 Richards-Kortum et al states that "we present **images** as they appear at the time of acquisition without any post-processing" and that "These images are representative of what would be possible for clinical applications requiring **near video rate imaging**..." (emphasis added)). One

having ordinary skill in the art would recognize that "near video rate imaging" constitutes image capture at a rate of multiple images per second. These multiple images acquired over time are displayed on a computer monitor (see col. 1, lines 47-54) which permit the clinician to monitor the intensity of light emitted from the tissue over time as recited by applicant in claim 6, line 6.

On page 16, first paragraph of paper no. 12, applicant states that since Richards-Kortum et al fail to teach or suggest methods which involve monitoring the intensity of light emitted from the tissue over time, an ordinary skilled artisan reading Richards-Kortum would not have been motivated to look for other methods of imaging tissue *in vivo* nor would the ordinarily skilled artisan have a reasonable expectation of success in arriving at applicant's invention. As explained in the preceding paragraph, Richards-Kortum et al does teach a method of monitoring the intensity of light emitted from the tissue over time. Accordingly, applicant's argument on page 16, first paragraph is moot.

On page 16, second paragraph of paper no. 12, applicant presents arguments regarding the rejection of claim 8 under 35 USC 103(a). Here applicant states that Richards-Kortum et al constitutes non-analogous prior art. Applicant notes that the method described in the instant application uses conventional 2-D macroscopic imaging of large surfaces of tissues whereas the method described by Richards-Kortum et al uses 3-D confocal imaging of smaller tissue areas. Two criteria have evolved for determining whether prior art is analogous: (1) whether the art is from the same field of endeavor, regardless of the problem addressed, and (2) if the reference is not within the field of the inventor's endeavor, whether the reference still is reasonably pertinent to the

particular problem with which the inventor is involved. In re Clay, 966 F.2d 656, 658-59, 23 USPQ 2d 1058, 1060 (Fed. Cir. 1992). See also In re Deminski, 796 F.2d 436, 442, 230 USPQ 313, 315 (Fed. Cir. 1986); In re Wood, 599 F.2d 1032, 106, 202 USPQ 171, 174 (CCPA 1979). In the present instance, one is informed by applicant's originally filed specification that the invention generally relates to a method for the *in vivo* diagnosis of a tissue abnormality in a subject by monitoring the intensity of light emitted from a tissue over time after contacting a tissue in a subject with a pathology differentiating agent. Since Richards-Kortum et al teaches a method for the *in vivo* diagnosis of a tissue abnormality in a subject by monitoring the intensity of light emitted from a tissue over time after contacting a tissue in a subject with a pathology differentiating agent, Richards-Kortum et al falls into the former category of the Wood test. Thus the examiner concludes that Richards-Kortum et al is analogous art.

Applicant traverses the rejection of claims 1-5 under 35 USC 102(e) as being anticipated by Kaufman et al (U.S. Patent Application Publication No. US 2002/0127735 A1) on the grounds that the Kaufman et al reference is not available as a 35 USC 102(e) reference in view of the declaration filed by applicant under 37 CFR 1.31. For the reasons given hereinabove, the declaration filed by applicant under 37 CFR 1.31 is incomplete and inadequate to establish possession of the invention. Therefore this declaration cannot be used to establish a date of invention prior to the effective filing date of U.S. Patent Application Publication No. US 2002/0127735 A1.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter P Nerbun whose telephone number is 703-308-0955. The examiner can normally be reached on M-F (1st Week) M-Th (2d Week).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John J Calvert can be reached on 703-305-1025. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0758 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0861.

Peter Nerbun
Primary Examiner

Peter Nerbun
February 2, 2003